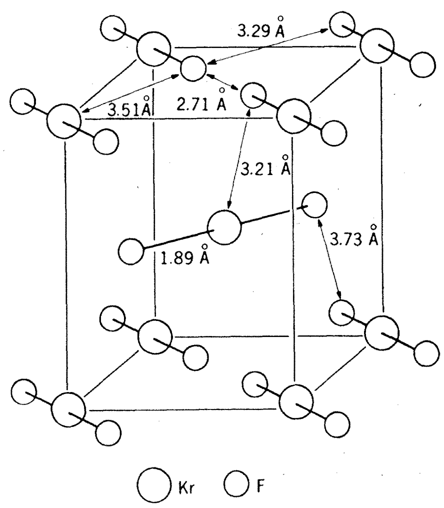

Fig. 1. Crystal structure and interatomic distances of KrF_2.

standard deviations are in parentheses.

Figure 1 illustrates the KrF_2 crystal structure. The linear molecules are aligned in planes perpendicular to the tetrad axes. The alignment alternates by 90° between successive planes. The Kr-F bond distance is 1.886 (0.021) Å. This may be compared with the gas phase electron diffraction value of 1.889 (0.010) Å (*8*) and the spectroscopic value of 1.875 (0.002) Å (*9*). The interatomic distances of interest are shown in Fig. 1. Each Kr atom has four F neighbors at 3.21 Å in adjacent planes and four F neighbors at 3.51 Å in the same plane. Each F atom has one close neighbor at 2.71 Å and two F neighbors at 3.29 Å in the same plane. Each F atom has eight neighboring F atoms at 3.73 Å in adjacent planes. The KrF_2 crystal structure presents an interesting contrast to the XeF_2 structure (*6*), in which the molecules are aligned parallel to the tetrad axes to form a body-centered arrangement (*10*).

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3. The crystal was subsequently lost by melting during an interruption in the liquid nitrogen supply.
4. Data collection was terminated at this point when the sample was lost during a malfunction of the cooling system.
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10. We have learned from S. Siegel that he and J. H. Holloway have obtained results similar to those reported here.

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Pancreatectomy in the Eel: Effects on Serum Glucose and Cholesterol

Abstract. *Pancreatectomy in the eel causes a slight tendency toward hyperglycemia; total and partial pancreatectomies cause a drop of total serum cholesterol. Thus, complete removal of the islet tissue in this teleost is not followed by diabetes mellitus, and also the endocrine control of the cholesterol-containing serum components seems to differ from that in mammals.*

The physiological role of the endocrine pancreas in fishes is very poorly understood (*1–4*), and the few data on pancreatectomy or isletectomy (*5, 6*) in teleosts are in part contradictory; in the latter, probably the only complete removal of all pancreas tissue was performed in the European eel, in which Caparelli, in 1894, found inconsistent glucosuria (*5*). All other authors removed the Brockmann bodies only, very likely leaving smaller islets with the remaining exocrine pancreas (*3*). Since the American eel (*Anguilla rostrata*) is the only teleost known to us to have all islet tissue concentrated in a compact pancreas (*7*), we studied the effects of pancreatectomy in this species on (i) serum glucose, as an indicator of diabetic alterations, and (ii) serum cholesterol, because of its high levels in some teleosts (*8*), in particular in the eel.

A total of 100 eels, ranging in weight from 36 to 108 g, were captured by net in the fall from freshwater near Philadelphia. Their coloration varied greatly, but all gonads were histologically undifferentiated. With regard to color, the animals were randomly distributed through the various experimental and control groups. For practical purposes, the animals were kept in aerated and filtered tap water at 14°C under dimmed continuous illumination. An acclimation period of several weeks was permitted before the surgical interventions, which started in December for the partially pancreatectomized animals (5 to 6 months group, Fig. 1), and all others in February ("winter-spring" animals). No food was given at any time. One additional group ($n = 9$) was captured in June and killed after 1 week in captivity ("summer controls"). Surgical techniques used were (i) total pancreatectomy, including partial removal of the portal vein (to be described in detail elsewhere); (ii) partial pancreatectomy by removal of approximately 40 percent of the pancreas from the caudal region, leaving the remaining tissue and the exocrine ducts intact; (iii) ligation of the portal vein between pancreas and liver; and (iv) an open-and-close sham operation. For surgery, the eels were anesthetized with Finquel (tricaine methonesulfonate). The wounds were closed with continuous nylon sutures. Beads were attached to the base of the dorsal fin to tag the animals. There was no postoperative mortality if the animals survived anesthesia and surgery for 12 hours, except for a few cases where sutures broke open. Unanesthetized animals were killed by decapitation immediately after removal from their containers, and uncontaminated blood, spurting from the ventral aorta, was collected in centrifuge tubes. Total serum cholesterol was determined colorimetrically with the Boehringer Mannheim test kit; serum "sugar" and serum glucose were determined enzymatically with the pertinent Boehringer Mannheim test kits (glucose oxidase and hexokinase methods, respectively). All total pancreatectomies were checked for pancreatic remnants after the animals were killed. All livers were checked macroscopically, histologically, and histochemically [Rossman's fixation at 4°C followed by aldehyde fuchsin with counterstains (*9*), or by Schiff's method for glycogen]; only two animals showed pathological liver alterations (partial necrosis), and these were excluded.

In all groups except the summer animals the values were obtained with the hexokinase method (Fig. 2). Both totally and partially pancreatectomized eels showed an initial hyperglycemia of approximately 350 and 180 percent, respectively, 1 day after the operation. By 3 days after, these groups had returned to the range of controls and continued in this range with a slight trend toward higher values, except for the partially pancreatectomized animals killed 18 to 20 days after the operation. After 1 day a mild hyperglycemia was also present in animals with portal vein ligations (about 200 percent). Six days after surgery, the serum glucose values of portal vein–ligated animals fell again within the range of the other groups, indicating that the initial hyperglycemia in the experimental groups was due to a stress reaction.

Very high levels of serum cholesterol (Fig. 1) were found in both control groups (normal values in humans, 180 to 250 mg/100 ml); however, they were almost 50 percent lower in the summer controls. The serum cholesterol concentrations of both totally and partially pancreatectomized eels dropped to a minimum at 12 to 20 days. After 5 to 6 months, there was a partial restoration toward the original values in the partially pancreatectomized eels. The sham-operated animals and the animals with ligation of the portal vein showed a slight decrease of the serum cholesterol after 1 day which, however, was statistically not significant; 6 days after portal vein ligation the values were normal.

At autopsy, considerable variations in the amounts of adipose tissue lipids were seen among controls as well as among the animals of individual experimental groups, with no trends apparent. No hyperlipemia was visible at any time in any serum sample.

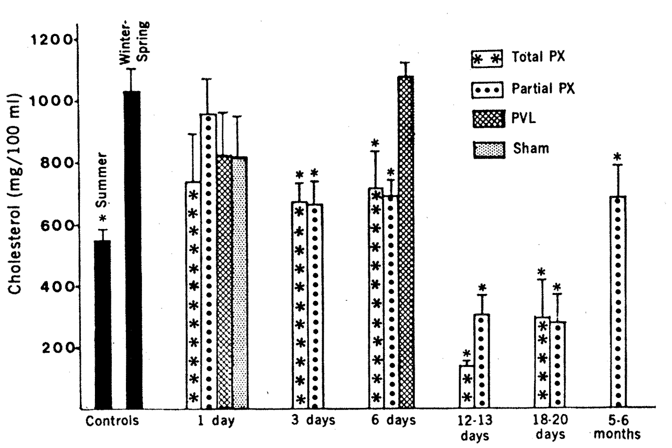
The great variations of blood sugar concentrations in teleosts, even under controlled conditions (*10*), and great variation from day to day without known reasons (*11*) indicate that a strict homeostatic control as in mammals is not present, at least in many species. The reported blood sugar values of 0 mg/100 ml or almost 0 mg/100 ml (*10*), furthermore, show the independence of teleost tissue from a given range of blood sugar concentrations. Thus, it is not surprising that our findings, obtained with the most specific method for blood glucose determination presently available, corroborate the 80-year-old data of Caparelli (*8*).

Our serum glucose values suggest that the importance of insulin and glucagon in carbohydrate metabolism of the eel is overshadowed by extrapancreatic factors. Our present studies (which will be published later) on liver glycogen are in good agreement with this, since we find no obvious differences between controls and pancreatectomized animals.

The total serum cholesterol values of our control group (captured in the fall) after more than 6 months without food intake were even higher than in freshly captured controls of the summer months. In rats, however, periods of starvation lead to a diminished cholesterol synthesis (*12*). The difference between the summer and winter controls may be due to seasonal variation (*13*) or an acclimation to the cold (*14*).

The lengthy period of food-free existence with high serum cholesterol concentrations shows that, in eels, food is not necessary for the maintenance of serum cholesterol concentrations; moreover, the fast drop of serum cholesterol after pancreatectomy indicates a relatively rapid turnover rate. Since the few data on teleosts indicate that a very high proportion of the serum cholesterol is bound to the lipoproteins (*15, 16*), it is very likely that the drop in cholesterol after the pancreatectomy reflects a decrease in the latter.

Teleosts have a negative feedback control for cholesterol synthesis, which involves exogenous cholesterol but not the endogenously produced serum component (*17*); consequently, the extremely high serum cholesterol concentrations of the nonfed eel could be due to this lack of control from its endogenous



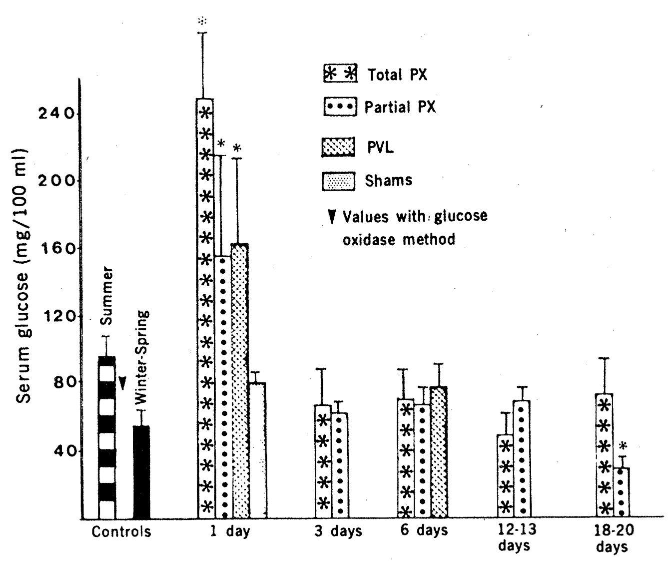


Fig. 1 (left). The effects of various surgical procedures on total serum cholesterol concentrations of the eel. After 3 days a drop in totally and partially pancreatectomized animals becomes obvious, and minimum concentrations are reached after 12 to 20 days. Portal vein ligation has no effect. Restoration toward the control values is found after 5 to 6 months in the partially pancreatectomized animals. A comparison with Fig. 2 shows that there is no correlation between the changes in serum glucose and cholesterol in the experimental animals. The possible inverse relation between concentrations of glucose and cholesterol in the intact control groups requires further studies. Statistical evaluation by *t*-test. The asterisk indicates values statistically different ($P < .05$) from the winter-spring controls. *PX*, pancreatectomy; *PVL*, portal vein ligation. Fig. 2 (right). The effects of various surgical procedures on serum glucose of the eel. Only severe surgical procedures (total and partial pancreatectomy, portal vein ligation) cause a transitory hyperglycemia. Therefore, partial pancreatectomy was used as the most meaningful control for possible unspecific effects of surgery. Intact controls ($n = 12$) of the winter-spring experiment were killed throughout the total duration of the study; since they showed no significant variations, they were grouped together. From 3 days on after the operation, only a slight but statistically not significant trend toward hyperglycemia is obvious in most groups. Statistical evaluation by *t*-test. The asterisk indicates values statistically different ($P < .05$) from the intact winter-spring controls. *PX*, pancreatectomy; *PVL*, portal vein ligation.

production. The effect of pancreatectomy on the serum cholesterol of the eel is the exact opposite of that found in mammals, including man, in which the operation is followed by increased concentrations of serum cholesterol (*18, 19*).

Since the animals had no food intake for months, one would assume that the drop in serum cholesterol is due to the removal of the endocrine pancreas. However, in severe human diabetes (*19*), as well as in experimental diabetes after B-cell cytotoxins (*20*), cholesterolemia is increased. Also, glucagon injections lower the cholesterolemia in mammals and lizards (*21*), and stimulates cholesterol breakdown into bile acids and glucose (*22*). From these findings in mammals and lizards, one would expect hypercholesterolemia in cases of insulin or glucagon deficiency, or both. On the other hand, it remains to be seen if in the eel the bile secretion, mucus, or sloughing cells of the digestive tract provide esterified cholesterol, whose uptake would partially depend on a pancreatic cholesterolesterase (*23*). In mammals the cholesterol in bile is found mainly in the free state (*24*), thus capable of recirculating via the enterohepatic pathway without esterase action, and most of the sloughing cells of the digestive tract are lost in the feces (*25*).

In mammals, only a very small amount of the pancreas is necessary to maintain the exocrine and endocrine secretion at effective levels (*26*). Since in all partially pancreatectomized animals we removed less than 50 percent of the gland, the tissue involved in the control of the cholesterolemia must have a rather small functional reserve. Further studies must show if the elevated concentrations of cholesterol in the partially pancreatectomized eels 5 to 6 months after the operation are due to regeneration of pancreas tissue or other compensatory mechanisms.

Finally, our results show that the total serum cholesterol of the eel is comprised of two fractions, one of which is pancrease dependent. The level of serum cholesterol at 12 to 20 days postoperative suggests that the pancreas-dependent fraction amounts to approximately 70 to 80 percent (Fig. 1).

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Recognition of Cancer in vivo by Nuclear Magnetic Resonance

Abstract. *Pulsed nuclear magnetic resonance has been used to differentiate in vivo between normal mouse tail tissue and a malignant transplanted melanoma, S91, located on the tail. The tumor displayed a nuclear (proton) spin-lattice relaxation time of ~0.7 second contrasted with the simultaneously measured normal tail tissue relaxation time of ~0.3 second.*

Measurements of the proton nuclear spin-lattice relaxation time T_1 have been shown by Damadian (*1*) and subsequently by others (*2*) to have different values in some normal biological tissues, benign tumors, and malignant tumors observed in vitro. These results raise the possibility of the application of nuclear magnetic resonance (NMR) to nondestructive detection and monitoring of tumors and their progressive growth in live animals, including humans. We report here the first studies in vivo with pulsed NMR to differentiate between the normal tissue of a mouse's tail and a transplanted malignant melanoma (known as Cloudman S91) without any obvious harm to the live animal. The data obtained were associated with two types of tissue, the normal with T_1 ~0.3 second and the malignant tumor with T_1 ~0.7 second. The trend of these numbers is in qualitative agreement with the earlier results in vitro (*1, 2*). Important differences between NMR measurement techniques in vitro and in vivo are geometric arrangements, motion of the animal, and the filling factor associated with the different tissues present.

It is necessary to place the part of the body being tested within a coil of wire (the "probe" coil), which in turn is situated in a strong magnetic field (*3*). Because of the size limitations of the available magnet, it was most convenient to perform this initial experiment on a mouse's tail, which had the advantage of being long and narrow

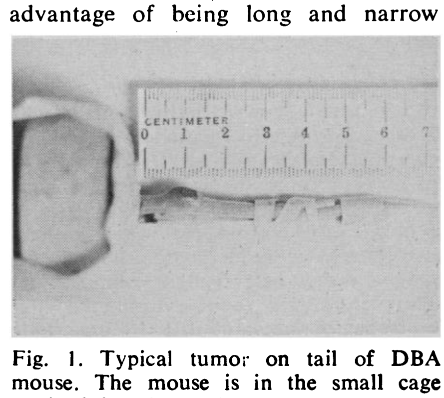

Fig. 1. Typical tumor on tail of DBA mouse. The mouse is in the small cage at the left (obscured).